REMARKS

Entry of the foregoing is respectfully requested. By the present amendment, claim 63 has been amended to recite the use of an additional antibody, thereby providing antecedent support for claim 64. Support for this amendment may be found in the specification and claims as originally filed. Furthermore, new claim 65 has been added. Support for newly added claim 65 may be found, at the very least, on page 44, line 28, to page 46, line 14; and on page 49, lines 25-29. No new matter enters by this amendment.

Rejection of Claim 64 Under 35 U.S.C. § 112, Second Paragraph

Claim 64 has been rejected under 35 U.S.C. § 112, second paragraph, for purportedly lacking antecedent basis for the limitation "the method of claim 63 wherein said second anti-ErbB2 antibody." By the present amendment, Claim 63 has been amended to recite a second anti-ErbB2 antibody. In light of this amendment to Claim 63, withdrawal of this rejection of Claim 64 under 35 U.S.C. § 112, second paragraph, should be reversed.

Rejection of Claims 28-31, 37-38, 40, 56 and 57 Under 35 U.S.C. § 102(b) or Alternatively Under 35 U.S.C. § 103(a)

In the Final Official Action mailed March 3, 2005, claims 28-31, 37-38, 40, 56 and 57 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Shepard *et al.*, or alternatively under 35 U.S.C. § 103(a) as allegedly being obvious over Shepard *et al.* Withdrawal of these rejections is respectfully requested.

"The mere fact that a disclosure...is found in a printed publication, does not make the disclosure itself any more meaningful to those skilled in the art (and thus, ultimately,

to the public). Rather, the criterion should be whether the disclosure is sufficient to enable one skilled in the art to reduce the disclosed invention to practice." In Re Borst 52 CCPA 1398, 1403 (CCPA 1965). "The test of whether a particular compound described in the prior art may have been relied upon to show that the claimed subject matter at issue would have been obvious is whether the prior art provided an enabling disclosure with respect to the disclosed prior art compound." Ashland Oil, Inc. v. Delta Resins & Refractories, Inc. 776 F.2d 281, 297 (Fed. Cir. 1985), citing In re Donohue, 766 F.2d 531, 533 (Fed. Cir. 1985).

Shepard *et al.* (a publication by the present inventors) identifies a panel of nine $p185^{HER2}$ monoclonal antibodies, which include both 7C2 and 7F3. Shepard *et al.* does not disclose the sequences of these antibodies, or provide any additional instruction as to how a skilled person could reproduce these particular antibodies. Furthermore, Shepard *et al.* does not suggest an antibody which binds to ErbB2 and results in about 5 to 50 fold induction of annexin binding relative to untreated cell in an annexin binding assay using B6474 cells. Therefore, Shepard *et al.* does not provide an enabling disclosure, as it does not enable one of skill in the art to produce the antibodies used in the claimed methods.

While the Examiner appears to accept that Shepard *et al.* does not provide an enabling disclosure, the Examiner argues that the Material Transfer Agreement (MTA) of Genentech does not preclude anyone in the public from obtaining the 7C2 and 7F3 antibodies if the public agrees to the conditions of the MTA. Therefore, the Examiner considers the antibodies to have been "publicly" available. Applicants respectfully disagree.

As noted in section 2133.03(a)(4)(B) of the MPEP, "'public use" of a claimed invention under 35 U.S.C. § 102(b) occurs when the inventor allows another person to use the invention without limitation, restriction or obligation of secrecy to the inventor." (emphasis added) In re Smith, 714 F.2d 1127, 1134, 218 USPQ 976, 983 (Fed. Cir. 1983). The key as to whether a disclosure to a third party constitutes public use lies in whether the inventor retains control over the use of the product as well as over the distribution of information concerning it. Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986). As noted in the Declaration of Phillips (submitted on December 18, 2002, and attached hereto as Exhibit A), any laboratory seeking to access the antibodies would have to be a bonafide research laboratory, and could not transfer this research material to others outside the laboratory receiving the research material. Furthermore, Genentech would have to approve of the proposed research plan, and the results of the research would have to be submitted to Genentech for review, recommendations and comments prior to receiving Genentech's approval for the outside investigator to make any disclosure of the research results. As is clear from the Declaration of Phillips, the present inventors clearly retained control over the use of the product as well as over the distribution of information concerning it. Thus, in accordance with MPEP section 2133.03(a)(4)(B), and contrary to the Examiner's assertion, the 7F3 and 7C2 antibodies were not publicly available.

Accordingly, it is respectfully requested that these rejections of Claims 28-31, 37-38, 40, 56 and 57 be withdrawn.

Rejection of Claims 28-31, 37-38 and 40 Under 35 U.S.C. § 102(b) or Alternatively Under 35 U.S.C. § 103(a)

Claims 28-31, 37-38 and 40 stand rejected under 35 U.S.C. § 102(b), for purportedly being anticipated by, or alternatively under 35 U.S.C. § 103(a), for purportedly being obvious in view of, Lewis *et al.* (Cancer Immunol. Immunother. 37:255-263 (1993)). For at least all of the reasons set forth below, withdrawal of these rejections are respectfully requested.

Again, "[t]he mere fact that a disclosure...is found in a printed publication, does not make the disclosure itself any more meaningful to those skilled in the art (and thus, ultimately, to the public). Rather, the criterion should be whether the disclosure is sufficient to enable one skilled in the art to reduce the disclosed invention to practice." In Re Borst 52 CCPA 1398, 1403 (CCPA 1965). "The test of whether a particular compound described in the prior art may have been relied upon to show that the claimed subject matter at issue would have been obvious is whether the prior art provided an enabling disclosure with respect to the disclosed prior art compound." Ashland Oil, Inc. v. Delta Resins & Refractories, Inc. 776 F.2d 281, 297 (Fed. Cir. 1985), citing In re Donohue, 766 F.2d 531, 533 (Fed. Cir. 1985).

Lewis *et al.* (also a publication by the present inventors) also discusses the 7C2 and 7F3 antibodies. Lewis *et al.* does not disclose the sequences of these antibodies, or provide any additional instruction as to how a skilled person could reproduce these particular antibodies. Furthermore, Lewis *et al.* does not suggest an antibody which binds to ErbB2 and results in about 5 to 50 fold induction of annexin binding relative to

untreated cell in an annexin binding assay using B6474 cells. Therefore, Lewis *et al.* does not provide an enabling disclosure.

While the Examiner appears to accept that Lewis *et al.* does not provide an enabling disclosure, the Examiner argues that the Material Transfer Agreement (MTA) of Genentech does not preclude anyone in the public from obtaining the 7C2 and 7F3 antibodies if the public agrees to the conditions of the MTA. Therefore, the Examiner considers the antibodies to have been "publicly" available. Applicants respectfully disagree, and cite to MPEP section 2133.03(a)(4)(B), as discussed above with respect to the Shepard *et al.* reference. Therefore, contrary to the Examiner's assertion, the 7F3 and 7C2 antibodies were not publicly available.

Accordingly, it is respectfully requested that these rejections of Claims 28-31, 37-38 and 40 be withdrawn.

Rejection of Claims 32-36, 39 and 58 Under 35 U.S.C. § 103(a) Over Shepard *et al.* or Lewis *et al.* in view of Fendly *et al.*, Deshane *et al.* and further in view of Senter *et al.*

Claims 32-36, 39 and 58 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Shepard *et al.* or Lewis *et al.* in view of Fendly *et al.*, Deshane *et al.* and further in view of Senter *et al.* In light of the following remarks, Applicants respectfully request withdrawal of this rejection.

As set forth above, neither Shepard *et al.* nor Lewis *et al.* anticipate or render obvious the method as set forth in Claim 28. Claims 32-36 and 39 either directly or indirectly depend on Claim 28. The Official Action has pointed to no teachings or suggestion in Fendly *et al.*, Deshane *et al.* or Senter *et al.* that remedies the above noted

deficiencies of Shepard *et al.* and Lewis *et al.* Specifically, none of these secondary references teach or suggest an isolated antibody that binds to an epitope on ErbB2 to which antibody 7C2 binds.

In addition, neither Shepard *et al.*, Lewis *et al.,* Fendly *et al.*, Deshane *et al.*, nor Senter *et al.*, alone or taken together, teach or disclose an isolated antibody that does not bind to an epitope on ErbB2 to which antibody 7C2 binds.

Furthermore, with respect to Claim 58, this Claim recites all of the limitations of Claim 28. Therefore, the arguments provided above regarding Claims 32-36 and 39 also apply to Claim 58.

In light of these remarks, it is clear that Claims 32-36, 39 and 58 are patentable over the cited references for at least the reasons set forth above with respect to Claim 28. Accordingly, it is respectfully requested that the rejection of Claims 32-36, 39 and 58 be withdrawn.

Rejection of Claims 42-55 and 59-62 Under 35 U.S.C. § 103(a) Over Shepard *et al.* in view of Lewis *et al.* and Fendly *et al.* and further in view of Deshane *et al.* and Senter *et al.*

Claims 42-55 and 59-62 have been rejected under 35 U.S.C. § 103(a) over Shepard *et al.* in view of Lewis *et al.* and Fendly *et al.* and further in view of Deshane *et al.* and Senter *et al.* For at least all of the reasons set forth below, withdrawal of this rejection under 35 U.S.C. § 103(a) is respectfully requested.

Initially, Claims 46-55 depend directly or indirectly from Claim 28. These claims are therefore also patentable over Shepard *et al.*, and Lewis *et al.* and Fendly *et al.* and further in view of Deshane *et al.* and Senter *et al.* for at least the reasons set forth above with respect to Claim 28 and with respect to Claims 32-36, 39 and 58.

Claim 42 recites a method for inducing cell death comprising exposing a cell which overexpresses ErbB2 to an effective amount of a composition comprising an antibody that binds to an epitope on ErbB2 to which antibody 7C2 binds and a pharmaceutically acceptable carrier. The antibody results in about 5 to 50 fold induction of annexin binding relative to untreated cell in an annexin binding assay using BT474. Claims 43-45 and 59-62 depend directly or indirectly from Claim 42.

Claim 42 differs from Claim 40 (discussed above) in that the antibody is present in a composition. Therefore, the arguments above with respect to Claim 40 also apply to Claims 42-45 and 59-62. Specifically, none of these secondary references teach or suggest an antibody that binds to an epitope on ErbB2 to which antibody 7C2 binds.

In light of these remarks, it is clear that Claims 42-55 and 59-62 are patentable over the cited references for at least the reasons set forth above with respect to Claims 28 and 40. Accordingly, it is respectfully requested that the rejection of Claims 42-55 and 59-62 be withdrawn.

Rejection of Claim 63 Under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) Over Shepard *et al.* or Lewis *et al.*

Claim 63 has been rejected under 35 U.S.C. § 102(b), for purportedly being anticipated by Shepard *et al.* or Lewis *et al.*, or alternatively under 35 U.S.C. § 103(a) for being unpatentable over Shepard *et al.* or Lewis *et al.* In light of the following remarks, Applicants respectfully request withdrawal of these rejections.

Initially, it is noted that neither Shepard *et al.* nor Lewis *et al.* disclose or suggest a method for inducing cell death comprising (1) exposing a cell which overexpresses ErbB2 to an effective amount of an isolated antibody that binds to an epitope on ErbB2,

wherein said isolated antibody induces cell death; and (2) exposing the cell to a second anti-ErbB2 antibody.

As noted above, Shepard *et al.* (a publication by the present inventors) identifies a panel of nine $p185^{HER2}$ monoclonal antibodies, which include both 7C2 and 7F3. Shepard *et al.* does not disclose the sequences of these antibodies, or provide any additional instruction as to how a skilled person could reproduce these particular antibodies or any antibodies that bind to ErbB2 and induce cell death. Therefore, Shepard *et al.* does not provide an enabling disclosure.

Lewis *et al.* (also a publication by the present inventors) also discusses the 7C2 and 7F3 antibodies. Lewis *et al.* does not disclose the sequences of these antibodies, or provide any additional instruction as to how a skilled person could reproduce these particular antibodies or any antibodies that bind to ErbB2 and induce cell death. Therefore, Lewis *et al.* does not provide an enabling disclosure.

Again, while the Examiner appears to accept that neither Shepard *et al.* nor Lewis *et al.* provide an enabling disclosure, the Examiner argues that the Material Transfer Agreement (MTA) of Genentech does not preclude anyone in the public from obtaining the 7C2 and 7F3 antibodies if the public agrees to the conditions of the MTA. Therefore, the Examiner considers the antibodies to have been "publicly" available. Applicants respectfully disagree.

As noted in section 2133.03(a)(4)(B) of the MPEP, "'public use" of a claimed invention under 35 U.S.C. § 102(b) occurs when the inventor allows another person to use the invention without limitation, restriction or obligation of secrecy to the inventor." (emphasis added) In re Smith, 714 F.2d 1127, 1134, 218 USPQ 976, 983 (Fed. Cir.

1983). The key as to whether a disclosure to a third party constitutes public use lies in whether the inventor retains control over the use of the product as well as over the distribution of information concerning it. Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986). As noted in the Declaration of Phillips (submitted on December 18, 2002, and attached hereto as Exhibit A), any laboratory seeking to access the antibodies would have to be a bonafide research laboratory, and could not transfer this research material to others outside the laboratory receiving the research material. Furthermore, Genentech would have to approve of the proposed research plan, and the results of the research would have to be submitted to Genentech for review, recommendations and comments prior to receiving Genentech's approval for the outside investigator to make any disclosure of the research results. As is clear from the Declaration of Phillips, the present inventors clearly retained control over the use of the product as well as over the distribution of information concerning it. Thus, in accordance with MPEP section 2133.03(a)(4)(B), and contrary to the Examiner's assertion, the 7F3 and 7C2 antibodies were not in public use.

Accordingly, it is respectfully requested that these rejections of Claim 63 be withdrawn.

Rejection of Claim 64 Under 35 U.S.C. § 103(a) Over Shepard *et al.* or Lewis *et al.* in view of Fendly *et al.*

Claim 64 has been rejected under 35 U.S.C. § 103(a) for purportedly being obvious in view of Shepard *et al.* or Lewis *et al.* in view of Fendly *et al.* For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Initially, Claim 64 depends directly or indirectly from Claim 63. This claim is therefore also patentable over Shepard *et al.*, and Lewis *et al.* for at least the reasons set forth above with respect to Claim 63.

The Official Action has pointed to no teachings or suggestion in Fendly *et al.* which remedies the above noted deficiencies of Shepard *et al.* and Lewis *et al.* Specifically, Fendly *et al.* does not teach or suggest an anti-ErbB2 antibody that does not bind to an epitope on ErbB2 to which antibody 7C2 binds.

In light of these remarks, it is clear that Claim 64 is patentable over the cited references for at least the reasons set forth above with respect to Claim 63. Accordingly, it is respectfully requested that the rejection of Claim 64 be withdrawn.

CONCLUSION

In view of the above amendment, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

MERCHANT & GOULD, P.C.

March 1, 2006
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